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Our objective is to use sodium MR imaging techniques to differentiate various breast tumor types in the rat. Specifically, we propose to determine and compare the sodium concentration and the T1 and T2 relaxation parameters for two rat breast tumor lines. Since sodium images have intrinsically low signal-to-noise ratios (SNR), the first part of this research involves implementing various methods to increase the SNR of sodium images. Three methods were proposed: use a higher field MR magnet, build an RF coil pair that transmits with a body coil but receives with a surface coil, and implement a filtered backprojection method of image acquisition and reconstruction. This part of the project is nearly complete. The coil pair has been built and tested successfully, and the MR scanner has been programmed to collect data to be reconstructed using the backprojection technique.

To verify that multiexponential decays exist in the tumors, a simple spectroscopy experiment was performed on three rats implanted with breast tumors. Biexponential decay was visible in the data, although there were large variations in the values of the decay constants, mostly likely due to susceptibility effects. This effect will not be a major factor in determining the relaxation parameters from the actual imaging experiments since spin echoes will be used for imaging.

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Hee Kwon Song / Sept. 29, 1995

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Table of Contents

Page	Item
1	Front Cover
2	SF 298 Report Documentation Page
3	Foreword
4	Table of Contents
5	Introduction
6	Methods and Developments
7	Results and Conclusions
8	References
10	Appendix A

Introduction

Reliable diagnosis of breast tumors is still in its developmental stages. Currently, mammography is widely used as a breast screening test, but is often unsuccessful in detecting and diagnosing tumors. It is difficult to detect tumors in women with dense breasts. Also, cancers that are located high in the breast and close to the chest wall are hard to detect with mammography. In addition, even if a lesion is discovered, it is difficult to determine whether it is malignant or benign since there is a considerable overlap in the tumors' shapes and densities. Biopsies are often necessary to determine the malignancy of detected tumors.

Magnetic resonance imaging (MRI) is becoming more popular as a diagnostic tool in breast cancer research. Although in the earlier years MRI had little to offer in the diagnosis of breast tumors over the less expensive mammogram, it is becoming more popular and promising as newer techniques are developed. The use of gadolinium (Gd) contrast agents has shown that malignant breast tumors consistently enhance, while benign lesions, such as scars and fat necrosis, do not. [1] More recently, "dynamic" contrast-enhanced MRI has been investigated. [2-8] In these studies, the investigators study not only the enhancement of the tumors, but also the *rate* of enhancement as contrast agents are injected into the patients. Studies show that cancerous tissue generally enhances faster than benign tumors. Some authors indicate, however, that these differences are not yet statistically significant and that other factors should also be considered in the final diagnosis. [7] Although studies with Gd-contrast agents have demonstrated that contrast-enhanced proton MRI has excellent sensitivity that exceeds that of mammography, the specificity still varies considerably. [9] Even with the use of these agents, it is still difficult to differentiate carcinomas from fibroadenomas; both tumor types often enhance by similar amounts. [10] Although MRI is more sensitive than mammography, used alone, it is not fully adequate for determining the malignancy of tumors.

The goal of this research is to investigate a different method to detect and characterize different types of breast tumors. It has been known over the years that sodium concentration is significantly higher in tumor cells than in normal cells. [11-17] X-ray microanalysis, NMR spectroscopy, and MRI experiments have demonstrated the increase in sodium (^{23}Na) content in neoplastic tissue. Because various cellular activities, including mitosis and oncogenesis, seem to depend heavily on cellular ionic concentrations and content, especially that of sodium, ^{23}Na MR imaging is potentially a more sensitive imaging technique than the conventional proton imaging method for both detection and differentiation of tumors. Sodium studies have been done in the past in both human and animal models, but no one has yet looked specifically into sodium MR imaging of different breast tumors and its potential to differentiate tumors without the need for more invasive techniques. The purpose of this research is to determine the sodium characteristics, including the concentration and T1 and T2 relaxation parameters, for two different types of rat breast tumors, 13762A and Ac33.

Sodium images have intrinsically low signal-to-noise ratios (SNR). Therefore, to acquire reliable quantitative data, we will combine three methods to increase the SNR of our images: use a higher field magnet; use a surface coil rather than a body coil during the receive mode; and implement a projection reconstruction technique to reduce the echo time. All of these techniques will aid in improving the SNR and in detecting all of the T1 and T2 components of the sodium signal.

Methods and Developments

The first step in improving the SNR of sodium images is by using a higher field MRI machine. A 4.7 Tesla animal imaging system has been installed in our laboratory. Previously, most of the animal studies have been done on the 1.9 Tesla animal imager. We can expect the signal-to-noise ratio to increase by a factor of about 2.5 with the new system, since SNR increases linearly with increasing field. We also have a six-inch inner diameter gradient set for the high field magnet. The set up is complete and has been proven to give high quality images in animal studies.

The second step was to build an RF coil that optimizes the SNR of our images. An RF coil pair has been constructed for this purpose. A linearly polarized birdcage coil for transmitting houses a smaller surface coil used to receive the signal. Since a smaller receive coil will pick up less noise than a larger one while being more sensitive to the region of interest, we can expect a significant increase in SNR. In order to decouple the two coils, they are oriented such that the rf field that each of them produces is orthogonal to the other. The surface coil is further decoupled from the transmit coil actively using a diode as described in literature. [18] The isolation between the two coils during RF transmission is 56 dB, and during receive (when decoupling is only passive) is 26 dB. Good images have been obtained in test studies.

The third way to increase the image quality is by reducing the echo time of our pulse sequence. Since the sodium signal decays exponentially after the spins have been excited, signal strength is strongest just after the RF pulse. Also, a short echo time is necessary in order to collect the fast component of T2 of sodium. To accomplish this, a pulse program for the MRI scanner implementing the backprojection algorithm was written and tested. The program consists of an initial 90 degree hard pulse followed by data collection. There is no phase encoding step as in conventional Fourier imaging. The data collection starts immediately following the RF pulse and is sampled with a constant interval throughout the readout period. During this period the gradients are in transition, and it is therefore necessary to interpolate the data points for accurate reconstruction. The program also collects data from subsequent spin echoes.

In order to reconstruct the collected data, a 3-dimensional filtered backprojection reconstruction algorithm was written in Pascal on the PC. The algorithm was tested successfully on both simulated data and real data from phantom imaging experiments. A simple linear interpolation was performed for data taken from the imaging experiments.

As a quick test for biexponential decay from sodium signals from the tumors, sodium spectroscopy was performed on the tumors in vivo. Ac33 rat mammary tumors were transplanted bilaterally into three rats. After two to three weeks the rats were anesthetized and spectroscopy was performed on the tumors. For two of the rats a single surface coil was used for spectroscopy, while for the third rat the new RF coil pair described above was used. Table 1 summarizes the results obtained from the experiments.

Results and Conclusions

The main goal of this period was to improve the quality (specifically, increase the SNR) of sodium images. RF coils optimized for sodium imaging of breast tumors were built, and filtered backprojection pulse program for the MRI scanner was implemented. Further work will involve modifying the sodium body coil to be able to obtain proton images as well. A well-known double tuning method using "tank circuits" can be used to accomplish this. [19]

From the Table 1, one can see that the standard deviations of the T2 values obtained from the spectroscopy experiments are large. This is probably due to local field inhomogeneities caused by susceptibility difference between air and tissue. Susceptibility effects will not be a major issue in the actual imaging experiments since spin echoes will be used to obtain the data for echoes two and above. The images from the first set of data points collected from the FID will also not be affected by susceptibility effects since the SNR depends primarily on the first few points of the data, which is collected before significant signal decay occurs.

The focus of the first year of the grant was on the implementation and construction of various tools necessary for successful sodium imaging experiments. Nearly all of the hardware and software needed to image rat breast tumors were built and written during this period.

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Appendix A

Table 1 Slow and fast components of sodium T2 values and their standard deviations in implanted rat breast tumors using MR spectroscopy.

	Average (ms)	**Standard Deviation (ms)**
T2 fast	2.4	1.13
T2 slow	8.5	5.60